SOME LITTLE APPRECIATED ASPECTS OF MALIGNANT LYMPHOMA.

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We are so accustomed to thinking of Hodgkin's disease and other forms of malignant lymphoma as typified by enlargement of the peripheral lymph nodes, and so accustomed to regarding leukemia as characterized mainly by a greatly increased white count and easy fatigue, that we sometimes forget that there are many other and important signs and symptoms of these diseases. Lymphoid tissue occurs normally in every organ of the body. Symptoms, therefore, of malignant lymphoma may be referred early or late in the disease to any organ, and the symptoms and signs may be most diverse and confusing. This point can be illustrated by referring briefly to the following cases.

Case 1—D. S. A married man of 48 years was admitted to the hospital in May, 1927. His chief complaint at that time was of epigastric pain, more common after meals, and intermittent diarrhea over a period of two years. This case might well have passed as a gastric ulcer. In addition to these symptoms he had noticed that for the past few months he tired more easily than usual and that in the past six months he had lost twenty pounds in weight, in spite of a good appetite. Physical examination was essentially normal, except that the spleen was palpable 4 cm. below the costal margin. There were constantly in the blood a few typical plasma cells, and the question was raised whether he might not have plasma cell leukemia. There were a few small nodes in each groin. One of them was excised, but showed merely chronic inflammation. An X-ray of the gastro-intestinal tract, however, revealed a large filling defect (plate 1), in the stomach. From an X-ray point of view this might well be either carcinoma or malignant lymphoma. The basal metabolism was +25, a laboratory finding more consistent with lymphoma than with cancer. In view of these findings a tentative diagnosis of lymphoma of the stomach was made. X-ray therapy brought about considerable

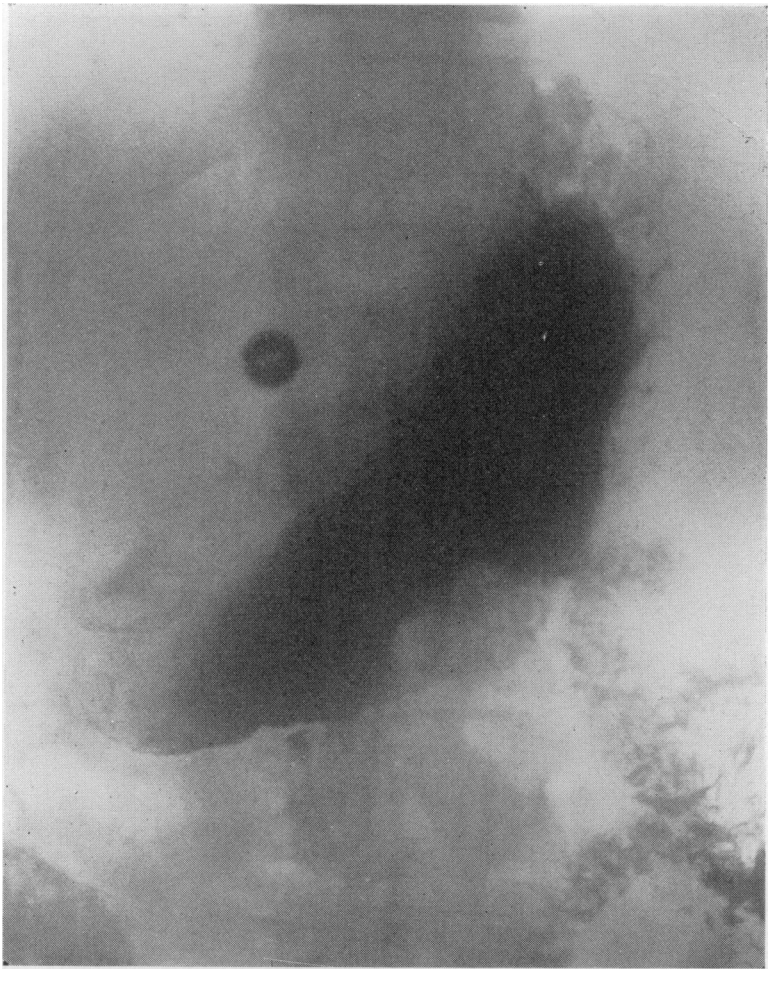

PLATE 1.

relief and though the symptoms recurred from time to time over the next four years they were correspondingly relieved by successive radiations. Finally in 1931 there was an acute exacerbation of symptoms and a physician in another state excised the diseased portion of the stomach. The specimen was by good chance sent to us for diagnosis. The lesion was typical Hodgkin's disease.

PLATE 2.

Case 2—R. C. A married engineer of 25 was admitted to the hospital in August, 1927. His chief complaint was itching all over the body and a swelling over the sternum. There were enlarged nodes in both sides of the neck and a smoothly rounded tumor of the upper sternum. Biopsy of the nodes in the neck showed Hodg-

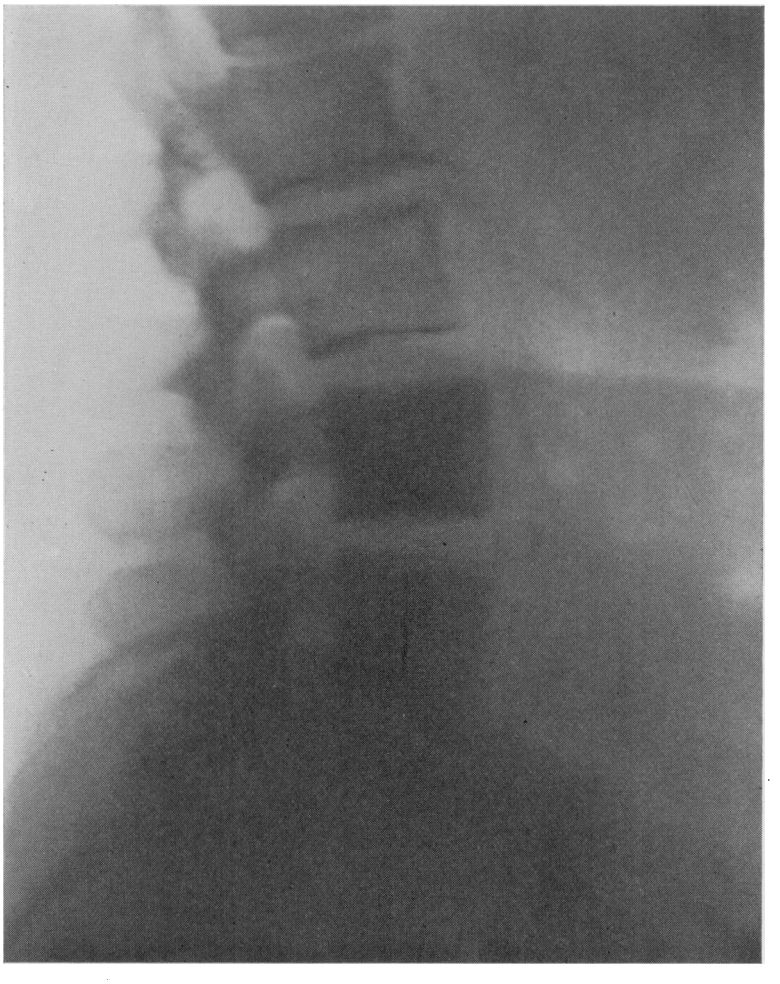

PLATE 3.

kin's disease and X-ray showed marked rarefaction of the sternum. It is to be noted that the patient was unaware of the lymph nodes in the neck. The disease was held in check by proper X-ray therapy until 1930, when the patient rather suddenly developed pain in his mid-back. X-ray (plate 2), showed a rarefaction of the sixth dorsal

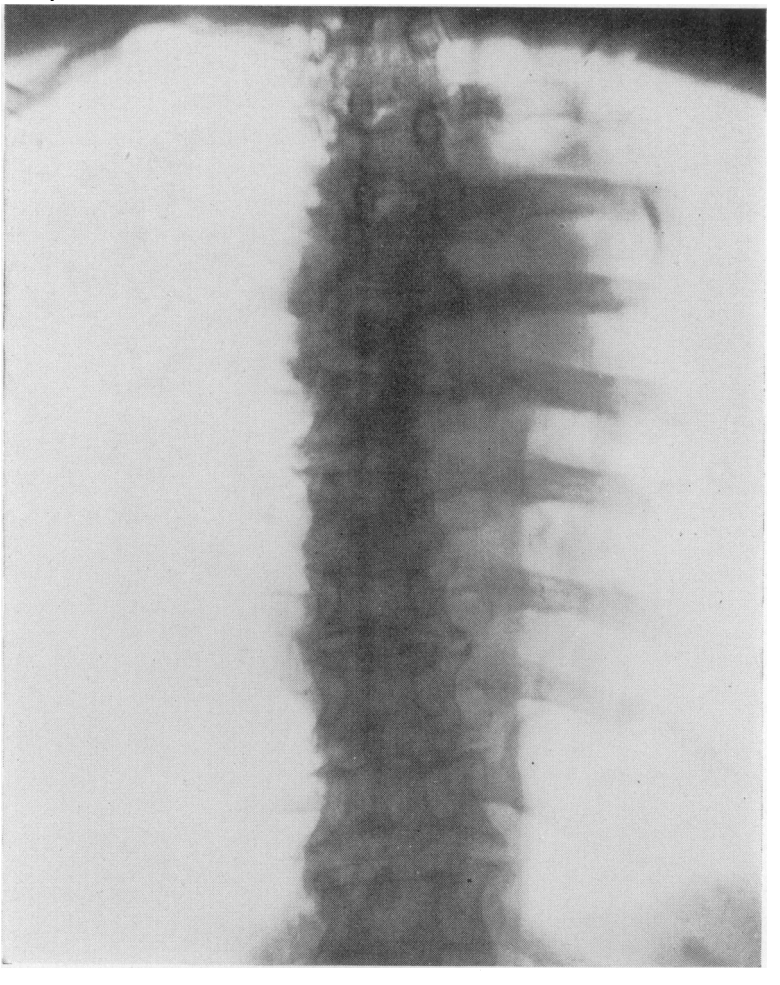

PLATE 4.

vertebra with collapse. The process in the spine extended and became progressively worse. Both legs became paralyzed and the patient suffered extreme pain. Contraction of both legs eventually set in and the patient died in 1932.

Case 3—N. P. A woman of 65 years was admitted in 1932 with a chief complaint of weakness and inability to walk. There was

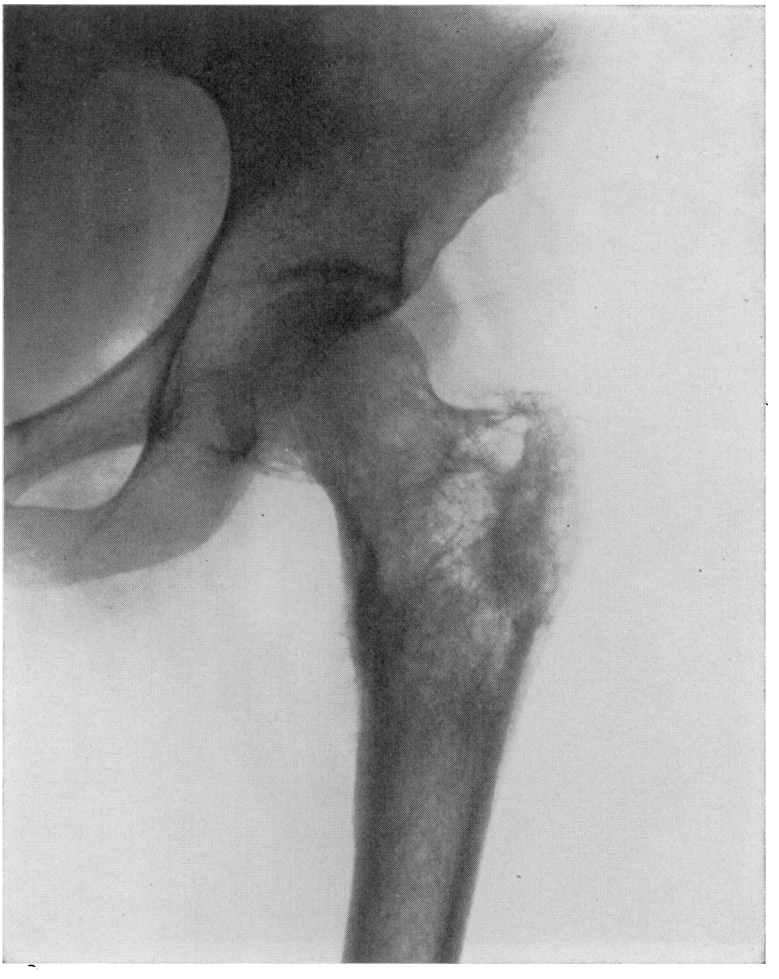

PLATE 5.

generalized peripheral lymphadenopathy and marked bronzing of the skin—a not rare sign of lymphoma. The right leg was spastic and there was a Babinski on the same side. There was a bilateral sustained clonus. X-ray studies showed (plates 3 and 4), a marked increased density of the third and fourth lumbar vertebrae and a destruction of the upper thoracic vertebrae, especially the sixth.

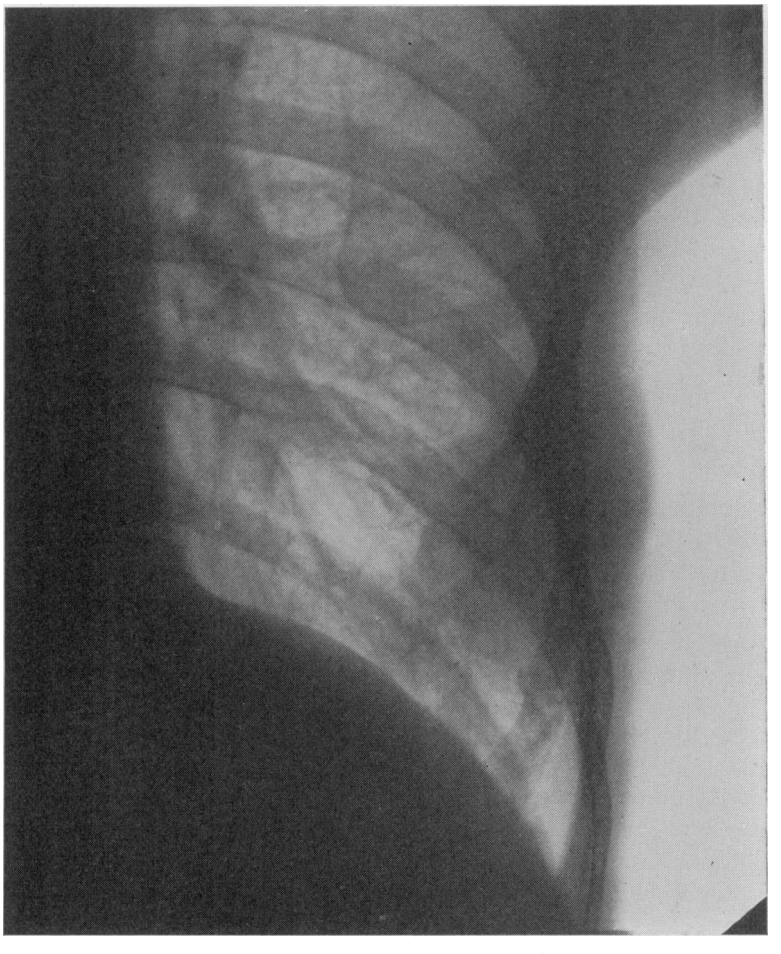

PLATE 6.

Case 4—A. W. A single American girl of 28 was admitted to the hospital in 1927. Her chief complaint was painless enlargement of the lymph nodes of the neck. Appropriate X-ray therapy brought about symptomatic relief for a period of four years. In 1931 she complained of severe pain in the right hip, the pain radiating down the leg to the dorsum of the foot. At this time there was no enlargement of the peripheral lymph nodes. The symptoms strongly sug-

gested an acute sacroiliac strain. X-ray showed (plate 5), an extensive destruction of the upper third of the femur. High voltage X-ray therapy to this region was followed by a prompt and lasting amelioration of symptoms. Today she is comfortable and in comparatively good health, though there is some stiffness of the right leg and she is unable to remain sitting for any great length of time.

Case 5—J. R. 51 years, male. The patient entered the hospital with enlargement of the submental glands. Pathological examination showed the condition to be Hodgkin's disease. A year later the patient experienced exquisite pain in the right lower chest after a trivial injury. An X-ray showed a pathological fracture of one of the lower ribs on this side with some callus formation (plate 6).

Case 6—E. G. An unmarried American girl of 23 entered the hospital with the chief complaint of exquisite pain and tenderness of the left wrist, both elbows and the left knee. There was marked redness, slight swelling of the affected parts. The heart was slightly enlarged and there was, all over the precordia, a harsh systolic murmur. The spleen was definitely palpable. There were no palpable peripheral nodes. Petechiae were found in the conjunctivae. There was marked pallor. The temperature was 101°—103°. The patient had been diagnosed malignant endocarditis by her personal physician. The white count on entrance was 32,000 with a great preponderance of lymphocytes with a not uncommon stem cell. The red count was 1,700,000. Platelets were absent. X-ray examination of the wrists showed destruction of the lower ends of the radius and ulnar (plate 7). The diagnosis was acute leukemia.

In malignant lymphoma and in leukemia there is not infrequently involvement of organs other than the lymph nodes. Bone involvement is common and requires very intensive treatment for its relief, lesions in the gastrointestinal tract are not rare; frequently they are the only or the main lesion. Cutaneous lesions are common and deceptive. Itching is particularly common. When the disease is manifest in the peripheral lymph nodes in the first instance the diagnosis is easy. But not infrequently the symptoms of which the patient complains at the onset are not those of glandular enlargement. We have seen a patient treated for a year as suffering from a traumatic knee joint, who actually had malignant lymphoma of the tibia.

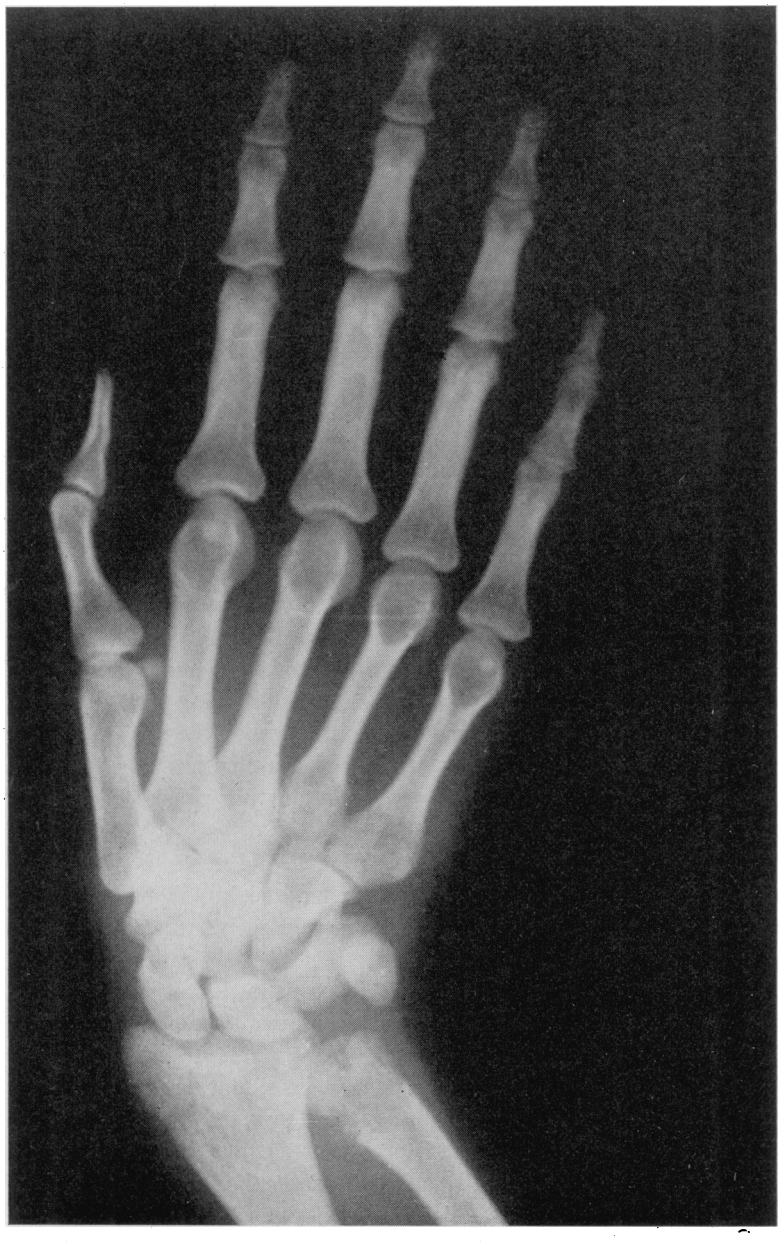

PLATE 7.

Not until two years after his initial symptoms did he develop peripheral lymph nodes. Fever, especially of the Pel-Ebstein type, may be the presenting symptom. In one such case which we have recently seen, peripheral lymph node enlargement occurred only after a year of intermittent attacks of unexplained fever. It behooves us, therefore, to remember that lymphoma and leukemia are diseases of protean manifestations or else the diagnosis may easily be missed.

DISCUSSION.

DR. O. H. PERRY PEPPER: Dr. Jackson has quite frankly said that he is not stressing the importance of what he has presented to you on the basis of its being new, but on the fact that we don't know what we should about such cases. What he has told us is well-known knowledge, is textbook knowledge one might say, but unfortunately most of us do not know what is in the textbooks, and certainly do not remember to apply it at the bedside.

We think of the pathology of Hodgkin's disease and realize that the Hodgkin's lesion may develop at any point in the body at which there are lymphoid deposits without our bothering to go into an argument as to whether is develops there by metastasis or otherwise. We are faced with a multutude of areas in which such lesions may develop.

The cases that he has recorded are cases that we can duplicate, I think, in almost any clinic with extensive experience. We have had a case of bone involvement whose skull picture could have been substituted almost for the one that Dr. Jackson showed.

The description in Osler's textbook of the bone lesion reads as follows: "Bone lesions may suggest osteomyelitis or bone tumor. There may be a granulomatous periostitis with osteophytes or rarefaction of the bone. The vertebrae are often involved, with a resulting pressure myelitis or pressure on the nerve roots. These cases may show very puzzling nervous symptom manifestations early in the course."

So it is merely to remind us of what we ought to know but don't, because we have never had a case of this kind come in that had not been diagnosed incorrectly repeatedly and which we also frequently diagnosed first incorrectly. Dr. Jackson has merely touched on the great variety of syndromes that this disease may produce. I think perhaps the most deceiving ones are those when the outstanding symptom is in the first place either anemia (because the anemia may be intense from the replacement of marrow by the granuloma) or where it is one of obstructive jaundice due to enlarged liver.

I think Dr. Jackson's presentation is most important to us in reminding us of the great variety of pictures that Hodgkin's disease may produce.

DR. CHARLES R. AUSTRIAN: I have been very much interested, as I am sure you all have been, in the presentation by Dr. Jackson of these relatively unusual manifestations of Hodgkin's disease.

I would like to say briefly one word because of the pass that I made to Dr. Jackson about an individual who came to one of the clinics in Baltimore some ten years ago, first with a manifestation of what seemed to be a paraplegia secondary to a tuberculosis of his spine. He showed during the course of observation the development of a telescoping of the spine which seemed to confirm the initial diagnosis. Then followed involvement of the lower spine with a formation of what seemed to be a sterile fluid and caused no tuberculosis when inserted into guinea pigs.

Another thing which he showed in addition to these manifestations was multiple osseous lesions scattered throughout the entire trunk and also involving the skull, the formation of some superficial abscesses on the body that were taken to be tuberculous at first but aspiration of which failed to confirm a diagnosis of tuberculosis, the formation then of a few enlarged nodes which showed in single glands, the formation of typical Hodgkin's tissue, and in other portions relatively normal glandular structure. The man went on to an uneventful end, and showed no evidences of tuberculosis that could be microscopically or otherwise demonstrated from the standpoint of bacterial or by animal inoculation.

DR. JACKSON: Dr. Pepper has referred to a number of the other confusing pictures, and perhaps I should have done a more complete job; it was merely, however, that I did not want to occupy too much of your time.

With this suggestion, however, I would like to point out one other type of confusing picture, and that is where fever is the primary symptom. We are all familiar, of course, with the Pel-Ebstein type of fever, as it is not an uncommon one and, in my experience, is not at all unlikely to be seen in those cases which have no periphereal glandular enlargement whatever.

I have recently seen such a case that, over a period of about eight months, ran an intermittent type of Pel-Ebstein fever which was absolutely undistinguishable by any peripheral enlargement at all, and it was only prior to death that he developed a few glands in the neck and a few in the axilla, and, that other point that he brought out, obstructive jaundice, about three weeks before his death.

Dr. Austrian asked me just before he got up whether I had seen any development of these abscesses, and I had gotten about to the point of saying "No" when he started to speak, and I remembered then that I had seen just last week a case very similar, or in fact almost identical, to the one that he spoke of, of a young boy of twenty who had a retraction of one limb, clean up on to his chest, with no glandular enlargement at all, very marked anemia, and before I left no X-ray diagnosis had been made, but I had learned that a biopsy had been done two years before for an obstructive tumor of the small intestine and that tumor had proved to be a Hodgkin's.

There is one further point that I believe I mentioned but which I would like to emphasize, and that is the development of the positive X-ray picture considerably follows the development of the actual lesion and the symptoms

coincident upon it, and therefore it is our custom to give X-ray treatment over areas which are painful but which do not subside under ordinary therapy of salicylates, hot packs, etc., even though the X-ray picture is negative. It has been our almost universal experience that when in the course of a few months or many months, perhaps, lesions have developed, these have justified our previous X-ray therapy. This should, however, be done only if some biopsy has previously made the diagnosis at least reasonably certain.